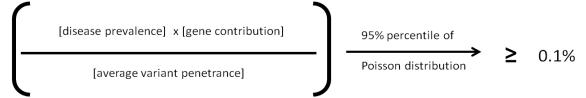
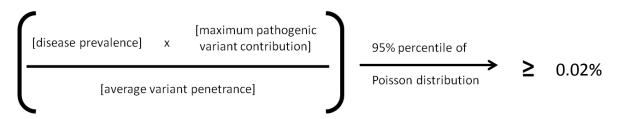
BA1 (MAF above which a variant can be classified as BENIGN assuming a MENDELIAN framework)



Assumptions (note: values deliberately set conservative to add "safety padding")

- **Disease prevalence**: Hypertrophic cardiomyopathy is traditionally estimated to occur in 1/500 individuals¹ though recent estimates suggest that is may be higher². Dilated cardiomyopathy was initially estimated to occur in 1/2,500 individuals but like HCM is now estimated to be much more common³. Therefore, 1/200 individuals (1/400 chromosomes) was used as a "safe" value.
- **Penetrance**: Although *MYH7* is generally regarded as a "penetrant" cardiomyopathy gene, this is not well characterized at the variant level and therefore, to accommodate all variants, a penetrance value of 30% was used.
- **Gene contribution** was set at 10.6% based on the detection rate for HCM, which is the highest among *MYH7* associated cardiomyopathies⁴.

BS1 (MAF too high for disease)



Assumptions

- Disease prevalence: 1/200 individuals (1/400 chromosomes)
- Penetrance: 30%
- Maximum pathogenic variant contribution: 2% based on MYBPC3 variant p.Arg502Trp (Walsh et al. 2017⁵: 6,000 probands)
- Note that the FAF (95% poisson) is available for each variant in ExAC (http://exac.broadinstitute.org/).

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